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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/485,267	01/23/2004	James Robert Murray	836.047	1718

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EXAMINER	
KANTAMNENI, SHOBHA	
ART UNIT	PAPER NUMBER
1617	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/485,267	MURRAY ET AL.	
	Examiner	Art Unit	
	Shobha Kantamneni	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 January 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *NONE* is/are allowed.

6)☒ Claim(s) *1-5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed on 01/18/2008, wherein claims 1-5 have been amended, and claims 6-7 have been cancelled.

Applicant's cancellation of claim 7, overcomes the objection made to claim 7.

Applicant's amendment overcomes the rejection of claims 1, and 3-6 under 35 U.S.C. 112, second paragraph, as being indefinite.

Applicant's amendment overcomes the rejection of claims 1-5 under 35 U.S.C. 112, second paragraph, as being indefinite.

Applicant's amendment overcomes the rejection of claims 1-5 under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process.

Claims 1-5 are examined insofar as they read on the elected invention.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, 4-5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of combating specific attention deficit disorder by employing a specific compound of formula I, galantamine does not

reasonably provide enablement for a method of combating attention deficit disorders by employing any compound represented by formula I, wherein said galantamine derivate is an acetylcholinesterase inhibitor that is active selectively at nicotine receptor sites. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant specification fails to provide information that would allow the skilled artisan to fully practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547, the court recited eight factors:

> (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1). The Nature of the Invention:

The rejected claims are drawn to an invention, which pertains to a method of combating attention deficit disorders, by the administration of a compound having the structures of formula I or formula II, whether said compound is effective as a acetylcholinesterase inhibitor that is active selectively at nicotinic receptor sites.

(2). Breadth of the Claims:

The complex nature of the subject matter of this invention is greatly exacerbated by the breadth of the claims. The claims encompass a method of combating attention deficit disorders by administering any compound having structures of formula I or formula II, whether said compound is effective as a acetylcholinesterase inhibitor that is active selectively at nicotinic receptor sites. The scope of the compounds claimed to be useful is extremely broad.

(3). Guidance of the Specification / (4). Working Examples:

AII of the guidance provided by the specification regarding combating attention deficit disorder is directed to merely one compound, galantamine.

(5). State of the Art / (6) Predictability of the Art:

The relative skill of those in the art is high with respect to combating attention deficit disorder by administering specific compound.

The invention is directed to a method of combating attention deficit disorders by administering any compound having structures of formula I, whether said compound is effective as a acetylcholinesterase inhibitor that is active selectively at nicotinic receptor sites. It is well established that the **scope of enablement** varies inversely with the degree of unpredictability of the factors involved, and physiological activity is generally considered to be an unpredictable factor. See In re Fisher, 427 F.2d 833, 839 (1970). It is further noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. The pharmacokinetic profile of a compound is governed by its physiochemical properties. The compounds of the instant invention of formula I have different functional groups and result in different biological

properties. More, polar compounds will have different properties such as different solubilities, binding abilities, different abilities to penetrate through cell membranes etc., then less polar compounds. For example, the compounds represented with the structure as in claim 1, formula I, will have different physiochemical properties. The compound of formula I, with R3 = CF3, will have different physical properties such as lipophilicity, binding abilities, solubilties, different ability to penetrate through cell membranes etc. than a compound with R3 = -OH, and thus will have different abilities to inhibit acetylcholinesterase or may lack the ability to inhibit acetylcholinesterase. Thus, in the instant case, the claimed invention is highly unpredictable, one of skill in the art is unable to fully predict possible physiological activities of any compounds represented by formula I, in the claimed method of combating attention deficit disorder. Moreover, one of the skills in the art would recognize that it is highly unpredictable with regard to therapeutic effects of the compounds herein, side effects such as adverse drug-drug interactions, serious toxicity that may be generated due to accumulation of drug itself or one of its metabolites. Thus, the instant claimed invention is highly unpredictable.

(7). The Quantity of Experimentation Necessary:

In order to practice the claimed invention, one of ordinary skill in the art would have to first envision a specific compound of the instant invention for the treatment, a dosage for each compound, the duration of treatment, route of treatment etc. One would then need to test the compound in the model system to determine whether or not the compound is effective as a acetylcholinesterase inhibitor that is active selectively at nicotinic receptor sites. One would then also need to test the compound in the model

system for side effects and toxicity at the site of pharmacological action and the therapeutic index of the drug. Thus a person of skill in the art would have to engage in undue experimentation to test these compounds encompassed in the instant claims to be administered to a host employed in the claimed methods of the particular treatments herein, with no assurance of success.

Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Snorrason (WO 92/20328, PTO-1449), in view of Gliichi (EP-0607864, PTO-1449).

Snorrason discloses the employment of cholinesterase inhibitor, galantamine, for the preparation of a pharmaceutical composition for counteracting the sedative or hypnotic or respiratory depressive effects of benzodiazepines (claim 1) given for the treatment of diseases such as hyperactivity of children. See claims 1, 17, 21-22, 27, and 39; page 4,

line 27. It is taught that acetylcholinesterase inhibitors are employed in combination with benzodiazepines (page 5, §1) in the treatment of attention deficit disorder e.g. hyperactivity of children to alleviate the undesirable side effects of the benzodiazepines. It is taught that galantamine is substantially selective at nicotinic receptor sides, and is capable of passing the blood-brain barrier in human. See page 7, lines 6-11.

Snorrason does not explicitly teach the employment of galantamine in the method of treating hyperactivity in children.

Gliichi teaches that acetylcholinesterase inhibitors can be employed in the treatment of attention deficit disorder, hyperkinesis. See page 71, lines 40-45.

It would have been obvious to a person of ordinary skill in the art at the time of invention to employ galantamine in the method of treating attention deficit disorder because 1) Gliichi teaches that acetylcholinesterase inhibitors are known to be used for treatment of attention deficit disorder, hyperkinesis, and 2) Snorrason teaches that galantamine is an acetylcholinesterase inhibitor. Accordingly, it would have been obvious to one of ordinary skill in the art to utilize the specific acetylcholinesterase inhibitor, galantamine for treating attention deficit disorder. One would have been motivated to utilize the specific acetylcholinesterase inhibitors because the combined references render the administration of an acetylcholinesterase inhibitor, in general, obvious. Accordingly, one would have had an expectation of similar success in treating attention deficit disorder by employing a specific acetylcholinesterase inhibitor, galantamine as instantly claimed.

Response to Arguments

Applicant argues that "the example data in Giichi demonstrate only that the tricyclic compounds have cholinesterase inhibitory activity and monoamine reuptake inhibitory activity. Giichi provides no rationale as to why the compounds might be useful to treat Huntington's chorea, hyperkinesis and mania, i,e, whether due to their cholinesterase inhibitory activity, due to their monoamine reuptake inhibitory activity, or due to some other activity of the tricyclic compounds". These arguments have been considered, but not found persuasive. It is pointed out that applicant is arguing against a single reference when the rejection was based on combination of references. Snorrason teaches that acetylcholinesterase inhibitors such as galantamine are employed in combination with benzodiazepines in the treatment of attention deficit disorder e.g. hyperactivity of children to alleviate the undesirable side effects of the benzodiazepines. Gliichi teaches that tricyclic compounds therein have acetylcholinesterase inhibitory activity and can be employed in the treatment of attention deficit disorder, hyperkinesis. Accordingly, it would have been obvious to one of ordinary skill in the art to utilize the specific acetylcholinesterase inhibitor, galantamine for treating attention deficit disorder. There is clear motivation to administer galantamine for treating attention deficit disorder because 1) galantamine is employed to alleviate side effects associated with benzodiazepines in treating attention deficit disorder, and 2) acetylcholinesterase inhibitors can be employed in the treatment of attention deficit disorder, hyperkinesis.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period, will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shobha Kantamneni whose telephone number is 571-272-2930. The examiner can normally be reached on Monday-Thursday, 8am-4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, Ph.D can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-272-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Shobha Kantamneni, Ph.D
Patent Examiner
Art Unit : 1617

/SREENI PADMANABHAN/
Supervisory Patent Examiner, Art Unit 1617

Application Number	Application/Control No.	Applicant(s)/Patent under Reexamination	
	09/485,267	MURRAY ET AL.	
	Examiner	Art Unit	
	Shobha Kantamneni	1617	